

IN THE CLAIMS:

Please amend the claims without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, as follows.

1. (Original) A pharmaceutical composition comprising:
an isolated heat shock protein (HSP) or heat shock protein-like protein (HSPLP), or a fragment thereof, in an effective amount to promote fugetactic activity and a pharmaceutically acceptable carrier.
2. (Original) The pharmaceutical composition of claim 1, wherein the HSP or HSPLP has a molecular weight of about 84 kDa.
3. (Original) The pharmaceutical composition of claim 1, wherein the HSP or HSPLP has a molecular weight of about 86 kDa.
4. (Original) The pharmaceutical composition of claim 1, wherein the HSP or HSPLP has a molecular weight of about 94 kDa.
5. (Original) The pharmaceutical composition of claim 1, wherein the HSP or HSPLP is a member of a heat shock protein (HSP) family selected from the group consisting of HSP60 (chaperonin), HSP70 and HSP90 families.
6. (Original) The pharmaceutical composition of claim 5, wherein the HSP or HSPLP is a member of the hsp90 family.
7. (Original) The pharmaceutical composition of claim 6, wherein the HSP or HSPLP is HSP 90 α .
8. (Original) The pharmaceutical composition of claim 6, wherein the HSP or HSPLP is HSP 90 β .

9. (Original) The pharmaceutical composition of claim 1, wherein the HSP or HSPLP comprises an amino acid sequence of SEQ ID NOs:3-7.
10. (Original) The pharmaceutical composition of claim 1, wherein the HSP or HSPLP is in a secreted form.
11. (Original) The pharmaceutical composition of claim 10, wherein the secreted form of the HSPLP comprises a signal sequence or a secretory sequence.
12. (Original) The pharmaceutical composition of claim 1, wherein the HSP or HSPLP is from a stressed or a non-stressed cell.
13. (Original) The pharmaceutical composition of claim 1, wherein the HSP or HSPLP is from a tumor or a tumor cell line.
14. (Original) The pharmaceutical composition of claim 13, wherein the tumor or tumor cell line is a hematological tumor or a hematological tumor cell line.
15. (Original) The pharmaceutical composition of claim 14, wherein the hematological tumor or hematological tumor cell line is a leukemia or a lymphoma.
16. (Original) The pharmaceutical composition of claim 15, wherein the lymphoma is a thymoma.
17. (Original) The pharmaceutical composition of claim 14, wherein the hematological tumor cell line is EL4.
18. (Original) A pharmaceutical composition comprising:

an isolated L-plastin or L-plastin-like protein (LPLP), or a fragment thereof, in an effective amount to promote fugetactic activity and a pharmaceutically acceptable carrier.

19. (Original) The pharmaceutical composition of claim 18, wherein the L-plastin or LPLP has a molecular weight of about 65 kDa.

20. (Original) The pharmaceutical composition of claim 18, wherein the L-plastin or LPLP is L-plastin.

21. (Original) The pharmaceutical composition of claim 18, wherein the L-plastin or LPLP comprises the amino acid sequence of SEQ ID NO:8.

22. (Original) The pharmaceutical composition of claim 21, wherein the L-plastin or LPLP is in a secreted form.

23. (Original) The pharmaceutical composition of claim 22, wherein the secreted form of the L-plastin or LPLP comprises a signal sequence or a secretory sequence.

24. (Original) The pharmaceutical composition of claim 18, wherein the L-plastin or LPLP is from a tumor or a tumor cell line.

25. (Original) The pharmaceutical composition of claim 24, wherein the tumor or tumor cell line is a hematological tumor or a hematological tumor cell line.

26. (Original) The pharmaceutical composition of claim 25, wherein the hematological tumor or hematological tumor cell line is a leukemia or a lymphoma.

27. (Original) The pharmaceutical composition of claim 26, wherein the lymphoma is a thymoma.

28. (Original) The pharmaceutical composition of claim 26, wherein the hematological tumor cell line is EL4.
29. (Original) A method of promoting fugetaxis of migratory cells in a subject, comprising:
administering to a subject in need of such treatment the HSP, HSPLP, L-plastin or LPLP of SEQ ID NOs:3-8, or a fragment thereof, in an amount effective to promote fugetaxis of migratory cells away from a specific site in a subject.
30. (Original) The method of claim 29, further comprising co-administering a non-fugetactic therapeutic agent.
31. (Original) The method of claim 30, wherein the non-fugetactic agent is an anti-inflammatory or an anti-allergic agent.
32. (Original) The method of claim 29, wherein the specific site is a site of an inflammation.
33. (Original) The method of claim 29, wherein the specific site is a medical device, prosthetic device or a transplanted organ or tissue.
34. (Original) The method of claim 33, wherein the medical device, prosthetic device or a transplanted organ or tissue is xenogeneic, stem-cell derived, synthetic or an allograft.
35. (Original) The method of claim 33, wherein the medical device, prosthetic device or a transplanted organ or tissue is a stent.
36. (Original) The method of claim 29, wherein the specific site is a site of an autoimmune reaction.
37. (Original) The method of claim 36, wherein the site of an autoimmune reaction is a site at or near a joint.

38. (Original) The method of claim 29, wherein the specific site is a site of an allergic reaction.
39. (Original) The method of claim 29, wherein the pharmaceutical composition is administered locally.
40. (Original) The method of claim 29, wherein the pharmaceutical composition is administered systemically.
41. (Original) The method of claim 29, wherein the HSP, HSPLP, L-plastin or LPLP is conjugated to a targeting molecule.
42. (Original) The method of claim 29, wherein the migratory cells are hematopoietic cells.
43. (Original) The method of claim 42, wherein the hematopoietic cells are immune cells.
44. (Original) The method of claim 43, wherein the immune cells are T cells.
45. (Original) A pharmaceutical composition, comprising:
an anti-fugetactic agent that selectively binds to a HSP, HSPLP, L-plastin or LPLP in an effective amount to inhibit fugetactic activity and a pharmaceutically acceptable carrier.
46. (Original) The pharmaceutical composition of claim 45, wherein the anti-fugetactic agent binds to an amino acid sequence of SEQ ID NOs:1-8 or a fragment thereof.
47. (Original) The pharmaceutical composition of claim 45, wherein the HSP or HSPLP has a molecular weight of about 84 kDa.

48. (Original) The pharmaceutical composition of claim 45, wherein the HSP or HSPLP has a molecular weight of about 86 kDa.

49. (Original) The pharmaceutical composition of claim 45, wherein the HSP or HSPLP has a molecular weight of about 94 kDa.

50. (Original) The pharmaceutical composition of claim 45, wherein the HSP or HSPLP is a member of a heat shock protein (HSP) family selected from the group consisting of HSP60 (chaperonin), HSP70 and HSP90.

51. (Original) The pharmaceutical composition of claim 45, wherein the HSP or HSPLP is a member of the hsp90 family.

52. (Original) The pharmaceutical composition of claim 51, wherein the HSP or HSPLP is HSP 90 α .

53. (Original) The pharmaceutical composition of claim 51, wherein the HSP or HSPLP is HSP 90 β .

54. (Original) The pharmaceutical composition of claim D1, wherein the L-plastin or LPLP has a molecular weight of about 65 kDa.

55. (Original) The pharmaceutical composition of claim 45, wherein the L-plastin or LPLP comprises an amino acid sequence of SEQ ID NO:8.

56. (Original) The anti-fugetactic agent of claim 45, wherein the anti-fugetactic agent is an isolated peptide.

57. (Original) The anti-fugetactic agent of claim 45, wherein the anti-fugetactic agent is an antibody or an antigen-binding fragment thereof.

58. (Original) The anti-fugetactic agent of claim 45, wherein the HSP, HSPLP, L-plastin or LPLP is in a secreted form.
59. (Original) The anti-fugetactic agent of claim 58, wherein the secreted form of the HSP, HSPLP, L-plastin or LPLP comprises a signal sequence or a secretory sequence.
60. (Original) The anti-fugetactic agent of claim 45, wherein the HSP, HSPLP, L-plastin or LPLP is derived from a tumor or a tumor cell line.
61. (Original) The pharmaceutical composition of claim 45, wherein the HSP or HSPLP is from a stressed or a non-stressed cell.
62. (Original) The pharmaceutical composition of claim 45, wherein the HSP, HSPLP, L-plastin or LPLP is from a tumor or a tumor cell line.
63. (Original) The pharmaceutical composition of claim 62, wherein the tumor or tumor cell line is a hematological tumor or a hematological tumor cell line.
64. (Original) The pharmaceutical composition of claim 63, wherein the hematological tumor or hematological tumor cell line is a leukemia or a lymphoma.
65. (Original) The pharmaceutical composition of claim 64, wherein the lymphoma is a thymoma.
66. (Original) The pharmaceutical composition of claim 63, wherein the hematological tumor cell line is EL4.
67. (Original) The pharmaceutical composition of claim 45, wherein the fugetactic activity is of hematopoietic cells.

68. (Original) The pharmaceutical composition of claim 63, wherein the hematopoietic cells are immune cells.

69. (Original) The pharmaceutical composition of claim 68, wherein the immune cells are T cells.

70. (Original) A method of eliciting or enhancing an immune response in a subject, comprising:

administering to a subject in need of such treatment the pharmaceutical composition of claim 45, in an amount effective to inhibit immune cell-specific fugetactic activity at a specific site in the subject.

71. (Original) The method of claim 70, wherein the specific site is a site of an allergic response.

72. (Original) The method of claim 70, wherein the specific site is a site of an infection.

73. (Original) The method of claim 70, wherein the specific site is a tumor.

74. (Original) The method of claim 70, wherein the pharmaceutical composition is administered locally.

75. (Original) The method of claim 70, wherein the anti-fugetactic agent is administered systemically.

76. (Original) The method of claim 75, wherein the heat shock protein is conjugated to a targeting molecule.

77. (Original) The method of claim 70, wherein the anti-fugetactic agent is geldanamycin, 17-A-GA, herbimycin A, PU3, novobiocin or radicicol.

78. (Original) A method of screening for an anti-fugetactic agent that modulates fugetaxis, comprising:

determining a control level of fugetactic activity by combining a migratory cell with a HSP, HSPLP, L-plastin or LPLP,

determining a test level of fugetactic activity by combining a migratory cell with the HSP, HSPLP, L-plastin or LPLP and a candidate compound, and

comparing the control and test levels of the fugetactic activity,

wherein a test level that is less than a control level indicates that the candidate compound is an anti-fugetactic agent.

79. (Original) The method of claim 78, wherein the migratory cell is an hematopoietic cell.

80. (Original) The method of claim 79, wherein the hematopoietic cell is an immune cell.

81. (Original) The method of claim 80, wherein the immune cell is a T cell.

82. (Original) A composition comprising:

an isolate from a thymoma cell line, wherein the isolate has fugetactic activity that is pertussis toxin inhibitable, protease degradable, and has a molecular weight of greater than about 5 kDa and is heat inactivatable.

83. (Original) The composition of claim 82, wherein the fugetactic activity of the isolate can be inhibited by heat inactivation at 56°C for one hour.

84. (Original) The composition of claim 82, wherein the fugetactic activity of isolate can be inhibited by proteinase K digestion at 37°C for one hour.

85. (Original) The composition of claim 82, wherein the isolate does not bind significantly to heparin.

86. (Original) The composition of claim 82, wherein the isolate binds significantly to a DEAE column in the presence of 20mM triethanolamine buffer and NaCl in a concentration lower than 0.25-0.5M.

87. (Original) The composition of claim 82, wherein the isolate is negatively charged at pH 7.5.

88. (Original) The composition of claim 82, wherein the fugetactic activity of the isolate can be inhibited by radicicol.

89. (Original) The composition of claim 82, wherein the production of the isolate by the thymoma cells can be inhibited by Brefeldin A.

90. (Original) The composition of claim 82, wherein the activity of the isolate is not significantly upregulated by heat shock at 42°C for one hour.

91. (Original) The composition of claim 82, wherein the molecular weight is greater than about 65 kDa.

92. (Original) The composition of claim 82, wherein the molecular weight is greater than about 80 kDa.

93. (Original) The composition of claim 82, wherein the molecular weight is greater than about 90 kDa.

94. (Original) The composition of claim 82, wherein the thymoma cell line is EL4.

95. (Original) The composition of claim 82, wherein the fugetactic activity is specific to T cells.
96. (Original) The composition of claim 95, wherein the T cells are cytotoxic T lymphocytes (CTLs).
97. (Original) The composition of claim 82, wherein the isolate is a substantially pure polypeptide.
98. (Original) The composition of claim 82, wherein the isolate is a supernatant of the EL4 thymoma cells.
99. (Original) The composition of claim 98, wherein the supernatant is diluted ten-fold.
100. (Original) A pharmaceutical composition comprising
the isolate of claim 82 in an effective amount to stimulate fugetaxis of a cell, and a pharmaceutically acceptable carrier.
101. (Original) The pharmaceutical composition of claim 100, wherein the fugetaxis is of an hematopoietic cell.
102. (Original) The pharmaceutical composition of claim 101, wherein the hematopoietic cell is an immune cell.
103. (Original) The pharmaceutical composition of claim 102, wherein the immune cell is a T cell.
104. (Original) The composition of claim 82, wherein the thymoma cell line is not undergoing significant apoptosis or necrosis.

105. (Original) The composition of claim 104, wherein the thymoma cell line is greater than 95% viable.

106. (Original) A method of producing a polypeptide having fugetactic activity from tumor cells comprising:

culturing the tumor cells at a density of 10^5 - 10^6 cells/mL in hybridoma serum free medium,

harvesting a supernatant from the tumor cells,

filtering the harvested supernatant with a 0.2 micron filter,

fractionating the filtered supernatant, and

analyzing the fractions for fugetactic activity.

107. (Original) The method of claim 106, wherein the tumor cells are a tumor cell line.

108. (Original) The method of claim 107, wherein the cell line is a thymoma cell line.

109. (Original) The method of claim 109, wherein the thymoma cell line is EL4.

110. (Currently amended) A polypeptide having fugetactic activity produced according to the method of ~~any one of~~ claims 106-109.

111. (Original) The polypeptide of claim 110, wherein the polypeptide has a molecular weight of about 84 kDa.

112. (Original) The polypeptide of claim 110, wherein the polypeptide has a molecular weight of about 86 kDa.

113. (Original) The polypeptide of claim 110, wherein the polypeptide has a molecular weight of about 94 kDa.

114. (Original) The polypeptide of claim 110, wherein the polypeptide has a molecular weight of about 65 kDa.

115. (Original) The polypeptide of claim 110, wherein the fugetactic activity is specific for hematopoietic cells.

116. (Original) The polypeptide of claim 115, wherein the hematopoietic cell is an immune cell.

117. (Original) The polypeptide of claim 116, wherein the immune cell is a T cell.

118. (Original) The polypeptide of claim 110, wherein the polypeptide is heat inactivatable and protease degradable.

119. (Original) The polypeptide of claim 110, wherein the fugetactic activity is pertussis toxin inhibitable.

120. (Original) The method of claim 110, further comprising culturing of the tumor cells so that the tumor cells are greater than 95% viable.

121. (Currently amended) A method of screening for an anti-fugetactic agent that modulates fugetaxis, comprising:

determining a control level of fugetactic activity by combining a migratory cell with the isolate of claim 82 ~~or the polypeptide of claim 106~~,

determining a test level of fugetactic activity by combining a migratory cell with the isolate of ~~any one of~~ claims 82 ~~or the polypeptide of claim 106~~, and a candidate compound, and comparing the control and test levels of the fugetactic activity,

wherein a test level that is less than a control level indicates that the candidate compound is an anti-fugetactic agent.

122. (Currently amended) The method of claim 121, wherein the ~~migratory~~ migratory cell is an hematopoietic cell.
123. (Original) The method of claim 122, wherein the hematopoietic cell is an immune cell.
124. (Original) The method of claim 123, wherein the immune cell is a T cell.